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CURRICULUM VITAE

Name: Larry I. Benowitz

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Place of Birth: Brooklyn, New York

Education:

1966 B.Eng. The Cooper Union, New York, NY

1973 Ph.D. California Institute of Technology, Pasadena, CA (Biology/Psychobiology; R.W. Sperry, thesis advisor)

Postdoctoral Training:

1973 Postdoctoral research fellow, Department of Biology, California Institute of Technology

1974-1975 Postdoctoral research fellow, Department of Psychology and Brain Sciences, Massachusetts Institute of Technology, Cambridge, MA

1975-1977 Research fellow, Department of Biological Chemistry, Harvard Medical School, Boston, MA (at McLean Hospital)

Academic Appointments:

1977-1979 Research Associate in Biological Chemistry, Harvard Med. School

1979-1987 Assistant Professor of Psychiatry (Psychobiology), Harvard Med School

1984- Associate, Program in Neuroscience, Harvard Medical School

1987-1990 Associate Professor of Psychiatry (Neuroscience), Harvard Med. School

1990- Associate Professor of Neurosurgery (Neuroscience), Harvard Medical School

Hospital Appointments:

1975-1977 Research Fellow in Biochemistry, McLean Hospital, Belmont, MA

1977-1979 Assistant Biochemist, McLean Hospital

1979- Associate Biochemist, McLean Hospital

1984-1990 Chief, Laboratory of Developmental Neurobiology and Neuropsychology, Mailman Research Center, McLean Hospital

- 1990- Director, Laboratory for Neuroscience Research in Neurosurgery,
Children's Hospital (Boston)
- 1990- Faculty Council, Awards Committee, Children's Hospital

Other Appointments:

- 1980 Visiting Scientist, The Open University, Milton Keynes, U.K.
- 1984-1987 Neuropsychology consultant for Positron Emission Tomography program, MGH
- 1985-1987 Consultant for National Aeronautics and Space Administration research project on space adaptation sickness.
- 1987-1989 Neurological Sciences Study Section, National Institutes of Health (ad hoc)
- 1991 Member, Visiting Committee, Neuroscience Program, Medical College of Pennsylvania
- 1997- Visual Sciences B Study Section, NIH (ad hoc, 1997-1999; Regular member, 2001-)
- 1996- Review panel, Whitehall Foundation

Assignments:

- 1979-1990 Chairman, Seminar Committee, McLean Hospital
- 1985-1988 Chairman, Boston Area Neuroscience Group (B.A.N.G.)
- 1987-1990 Institutional Animal Care and Use Committee, McLean Hospital
- 1988 Planning Committee, National Eye Institute, NIH, Bethesda, MD
- 1988-1997 Admissions Committee, Program in Neuroscience, Harvard Med.
- 1988- Advisory Committee, Program in Neuroscience, Harvard Med. Sch
- 1989-1990 Teaching and Education Committee, McLean Hospital
- 1990- Faculty Council, Children's Hospital
- 1994 Review Panel, Howard Hughes Medical Institute (Research Training Fellowships)
- 1994 Reviewer, Medical Research Council of Canada
- 1995-1997 Chair, Human Resources Subcommittee, Children's Hospital
- 1995- Faculty Advisor, William Castle Society, Harvard Medical School
- 1996 Local Host Committee Annual Meeting, Society for Neurochemistry
- 1998- Co-chair, Committee on Awards and Honors, Harvard Med School

Memberships in Professional Societies:

- 1965- Tau Beta Pi (honor society in engineering)
- 1972- A.A.A.S.

- 1973- Society for Neuroscience
1987- American Society for Neurochemistry
1991- Boston Society for Neurology and Psychiatry

Editorial assignments:

Editorial Board of *Brain Research*

Frequent reviewer for *J. Neurosci.*, *Exper. Neurol.* occasional reviewer for *Nature*,
Science, *Neuron*, *J. Neurochem*, *PNAS*, *J. Comp. Neurol*, others

Awards and Honors:

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| 1962-1966 | New York State Scholarship |
| 1966-1967 | Atlantic Richfield Fellow in Chemistry and Chemical Engineering |
| 1974-1975 | NIH Postdoctoral Fellowship |
| 1975-1976 | Medical Foundation Fellowship |
| 1976-1977 | Scottish Rite Fellowship |
| 1978-1980 | Alfred P. Sloan Foundation Fellowship |
| 1980 | Harvey Shein Award, McLean Hospital (First prize, submitted paper) |

Other Activities:

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| 1990 | Fundraising, Operation Exodus |
| 1990-1992 | Fundraising, The Medical Foundation, Boston, Massachusetts |

Research, Teaching, Clinical Contributions:

A. Narrative Report. My primary research goals are to understand the mechanisms that control the growth of neural connections and to translate this work into improving outcome after CNS injury. At the cellular/molecular level, we have identified novel molecules that stimulate axon outgrowth, and investigated the intracellular signaling pathways involved and resultant changes in gene expression. *In vivo*, our research focuses on stimulating axon growth in the injured spinal cord, enhancing the reorganization of brain connections after stroke, and stimulating axon regeneration in the optic nerve. We recently identified one small molecule (AF-1) that enables lower vertebrates to regenerate their optic nerves, and found that same molecule is present in mammals, where it may serve as a co-activator of axon growth. In the mature optic nerve, nerve injury normally results in no axon regeneration and the apoptotic death of retinal ganglion cells. If we stimulate an inflammatory reaction in the eye, many ganglion cells survive axotomy and regenerate axons through the normally inhibitory terrain of the optic nerve. We have identified a macrophage-derived protein which, acting synergistically with AF-1, appears to mediate this growth. Applying this protein via slow-release polymers may eventually benefit victims of glaucoma and others suffering from CNS injury. Another small molecule that induces axon outgrowth is the purine nucleoside inosine. Inosine activates a protein kinase that controls the expression of a set of downstream genes important for axon growth. In mature rats, we found that after a unilateral injury to the corticospinal tract, inosine stimulates axons in the undamaged tract to form collateral branches that cross from the intact side of the spinal cord to form connections in the half which had lost its normal inputs. We have extended these studies to show that inosine promotes the growth of new brain connections after a stroke, leading to improvements in functional outcome. Phase I/II clinical trials using inosine in stroke victims will begin soon. One protein that is involved in the plasticity of neural connections is GAP-43, of which we were co-discoverers >20 years ago. GAP-43 expression is partly regulated by a post-transcriptional mechanism, and we have identified the *trans*-acting factor that mediates control of GAP-43 mRNA stability. We are using microarrays to discover other components of the neuron's axonal growth program.

I serve as Co-chair of Harvard Medical School's Committee on Awards and Honors and am a member of the Harvard Program in Neuroscience Steering Committee and the Research Faculty Council at Children's. I am the Course Director of the Advanced Topics in Neuroscience series at Harvard Medical School and have taught several courses in this series. I have also lectured in other courses at the medical school. I have served as mentor for many graduate, medical, and postdoctoral students, and served on many thesis committees (advisory, prelim., final). I am a member of the Visual Sciences B Study Section at the NIH, principal reviewer for molecular neuroscience of the Whitehall Foundation, and a frequent reviewer for journals.

B. Funding information

Current Funding

Years	Funding source	Role	Grant title
1979-	NIH (EY 05690)	PI	Molecular Bases of Neural Connectivity
1995-	Boston Life Sci. Inc.	PI	Clinical applications of novel growth factors
2001-2004	NIH (R29 NS41996)	PI	Role of Purine Nucleosides in CNS Regeneration
2002-2004	Glaucoma Foundation	PI	Replenishing retinal ganglion cells and inducing axon growth in an experimental model of glaucoma

Past Funding

1977-1980	NIH (NS 14647)	Co-PI	Biochemical correlates of neural regeneration
1984-1986	American Paralysis Assn	PI	Molecular Bases of Neural Regeneration
1986-1987	Marion Benton Trust	PI	Molecular Bases of Brain Development
1986-1988	Whittaker Hlth. Sci. Fund	PI	Bioactivity and characterization of factors from injured lower vertebrate CNS that promote outgrowth of mammalian CNS neurons
1986-1989	NIH (R01 NS25830)	PI	GAP/B50: A Molecular Marker of Neuronal Plasticity
1997-1998	NIH	PI	Special Research Award on Nerve Regeneration
1988-1990	Scottish Rite	PI	Molecular Specializations of the Association Cortex in Normal and Schizophrenic Subjects
1999-2001	Christopher Reeve the Paralysis Foundation	PI	Purine nucleoside stimulation of axon growth in injured corticospinal tract
1999-2001	Glaucoma Research Fndn.	PI	Retinal Ganglion Cell Survival and Axon Regeneration after Optic Nerve Damage
2000-2001	Amyotrophic Lateral Scler Therapy Devel. Fndn.	PI	Innovative therapies in mouse ALS model

C. Current Research Activities

Project	Role
Signal transduction pathways in axon growth	PI
Axon regeneration in the adult mammalian optic nerve	PI
Rewiring the brain and improving functional outcome after stroke	PI
Enhancing axon growth after spinal cord injury	PI
Molecular changes underlying axon regeneration	PI
Use of stem cells to replace retinal ganglion cells after stroke	PI

D. Teaching

- 1968-1973 Lectures and laboratory demonstrations in animal behavior, physiological psychology, psychoanalytic theory of dreams, Department of Biology, California Institute of Technology.
- 1974-1989 Lectures in neuroanatomy, animal behavior and learning, human neuropsychology, neurochemistry, neural development, Harvard Medical School, Harvard College, and M.I.T.
- 1975 Speaker and Participant, Gordon Conference on Neural plasticity
- 1977-1979 Organizer and participant in weekly seminars on biological bases of human behavior for Residents, McLean Hospital
- 1981-1985 Participant in behavioral neurology rounds, Mass. Rehabilitation Hospital
- 1985 Speaker and Participant, Gordon Conference on Neural plasticity
- 1985 Lecturer, Neuroscience for Neurosurgeons, MBL, Woods Hole, MA
- 1985-1990 Co-organizer of course on biological psychiatry for senior residents in psychiatry, McLean Hospital
- 1985-1997 Lectures, Biological Bases of Mental Retardation (2 per year every second year)
- 1988-1990 Tutor, Human Nervous System and Behavior Course, Harvard Medical School (weekly tutorial sessions, 6 hours/week, 1 term/year)
- 1989 Invited Lecture, Cornell University Medical College, Department of Physiology
- 1990 Neurobiology and Behavior Course, McLean Hospital (Co-organizer)
- 1990 First invited lecturer, U. Michigan Neuroscience Retreat
- 1990 Grand Rounds, Department of Neurology, Beth Israel Hospital, Boston, Massachusetts
- 1990-1994 Training Grant Committee, Children's Hospital
- 1991-1993 Lecturer, Neurobiological Basis of Behavior, McLean Hospital (one lecture per year)
- 1991-2002 Course Director, Advanced Topics in Neurobiology, Harvard Medical School. Presented half-semester courses to graduate students and postdoctoral fellows (2 hrs/week): "Cellular and Molecular Aspects of Nerve Regeneration" (1991), "Functional Organization of the Human Brain (1995); Nerve regeneration: cellular and molecular aspects (1997); Cellular and molecular aspects of nerve regeneration (2002). Average section had 10-15 students per term.
- 1993 Mentor, Research Science Institute, MIT

- 1994- Faculty advisor, Four Directions Summer Research Program/Native American Health Organization
- 1994 Speaker, Workshop on Effective Teaching Formats, Harvard Medical School
- 1994-1997 Lecturer and Participant, Development of Mind, Brain, and Behavior, Harvard University
- 1994-1995 Lecturer and Participant, William James Society, Harvard Medical School
- 1996 Grand Rounds, Combined Neurology Program, Harvard Medical School
- 1999-year) Lecturer, HST130 (Introduction to Neuroscience: 1 lecture per year)
- 2000 Grand Rounds, Department of Neurosurgery BWH, Children's Hospital
- 2000- Board of Honors Tutors, Harvard University

Regional, national or international contributions

- 1986 Co-Chairman, NRP Conference on "A key phosphoprotein in neuronal development and plasticity," Neuroscience Institute, Rockefeller University (with B. Grafstein, A. Routtenberg), 4/86
- 1986 Invited lecture, Department of Biology, McGill University, Montreal, Canada
- 1986 Invited lecture, SUNY Buffalo
- 1986 Symposium speaker, Axonal Transport Conference, University of Calgary, Alberta, Canada
- 1987 Invited lecture, Cornell University Medical College
- 1987 Invited lecture, Rutgers University
- 1987 Invited lecture, MGH Department of Neurology
- 1987 Invited speaker, Aphasia Research Center, B.U. School of Medicine
- 1988 Invited speaker, Johns Hopkins University, Baltimore, Maryland
- 1988 Invited lecture, Nathan S. Kline Inst. for Psychiatric Research, Orangeburg, NY
- 1988 Invited lecture, Dept. Neurobiology, Yale University School of Medicine
- 1988 Invited lecture, Duke University
- 1989 Invited speaker, University of Medicine and Dentistry of New Jersey
- 1989 Invited lecture, Dept Anatomy, Medical College of Pennsylvania, Philadelphia
- 1989 Symposium speaker, Regulators of Peripheral Nerve Regeneration, Ystad, Sweden

- 1989 Invited speaker, Tufts University School of Medicine
- 1989 Symposium speaker, Molecular and Cellular Mechanisms of Neuronal Plasticity in Aging and Alzheimer's Disease, NIH, Bethesda, Maryland
- 1989 Invited lecture, Department of Biology and Biochemistry, Brandeis University
- 1989 Invited speaker, Department of Brain and Cognitive Sciences, MIT
- 1990 Inaugural speaker, University of Michigan Program in Neuroscience Annual Retreat
- 1990 Symposium speaker, Third International Phosphoprotein Conference, Utrecht, The Netherlands
- 1990 Invited speaker, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY
- 1991 Seminar speaker, Neuroscience Graduate Program, Tufts University, School of Medicine
- 1991 Invited lecture, Department of Neurology, VA Medical Center, UCLA, Los Angeles, CA
- 1991 Invited lecture, E.K. Shriver Center, Waltham, MA
- 1992 Invited lecture, Montana State University, Bozeman, MT
- 1992 Seminar speaker, Massachusetts General Hospital, Boston MA
- 1992 Invited speaker, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School
- 1993 Symposium speaker, International Congress of Physiological Sciences, Glasgow, Scotland
- 1993 Invited lecture, University College, London, Great Britain
- 1993 Invited lecture, INSERM, Orsay, France
- 1994 Invited lecture, McLean Hospital
- 1994 Symposium speaker, American Society for Neurochemistry, Albuquerque, New Mexico
- 1994 Invited lecture, Senior Society of the American Academy of Neurosurgeons, Naples, FL
- 1994 Symposium speaker, XXXII International Congress of Physiological Sciences, Scotland.
- 1994 Symposium speaker, Oklahoma Center for Neuroscience, University of Oklahoma, Oklahoma City, Oklahoma
- 1994 Invited speaker, Brigham and Women's Hospital, Harvard Medical School
- 1994 Symposium speaker, American Psychological Association: Tribute to Roger Sperry, Los Angeles, California
- 1994 Invited speaker, Harvard Medical School, Department of Genetics
- 1994 Invited speaker, Harvard Medical School, Department of Neurobiology

- 1994 Symposium speaker, Activity-Dependent Changes in Synaptic Organization, New York
- 1994 Symposium speaker, Synaptic Plasticity and Aging, NIH, Bethesda, Maryland
- 1995 Symposium speaker, Senior Society, Society of Neurological Surgeons, Boston, Massachusetts
- 1995 Invited lecture, University of Utrecht (Netherlands)
- 1995 Invited lecture, University of Leuven (Belgium)
- 1995 Invited lecture, McLean Hospital
- 1996 Principal lecture, Boston Area Neuroscience Group, Annual Meeting
- 1996 Invited lecture, Columbia University
- 1996 Invited lecture, Harvard University, Mind, Brain and Behavior series
- 1996 Invited lecture, University of Massachusetts
- 1997 Invited lecture, Institute of Ophthalmology, University College, London
- 1997 Invited lecture, Department of Anatomy, University College, London
- 1997 Invited lecture, Department of Biology, University of Konstanz, Germany
- 1997 Invited lecture, Department of Development and Evolution of the Nervous System, École Normale Supérieure, Paris
- 1997 Invited lecture, Dept. of Neurobiology, Harvard Medical School
- 1997 Invited Lecture, Department of Biology, Boston College
- 1997 Chair, Session on Regeneration, Annual Meeting, Society for Neuroscience, New Orleans, Louisiana
- 1998 Invited lecture, University of Michigan
- 1998 Invited lecture, State University of New York (Albany)
- 1998 Invited lecture, Boston College
- 1998 Symposium organizer and speaker, 12th biennial meeting, International Society for Developmental Neuroscience, Vancouver, B.C., Canada
- 1998 Invited lecture, University of Louisville (KY)
- 1998 Inaugural lecture, Neuroscience Series, University of Medicine and Dentistry, New Jersey
- 1998 Symposium speaker, University of Heidelberg (Germany)
- 1998 Symposium speaker, Retinal ganglion cell death in glaucoma, Val-Morin, Quebec, Canada
- 1998 Symposium organizer and speaker, European Society for Neurochemistry (St. Petersburg, Russia)
- 1999 Inaugural Lecture, Restorative Neurology Seminar Series, UCLA

- 1999 Symposium Speaker, Developments in CNS Drugs: Drugs of Tomorrow conference in London, UK
- 1999 Invited lectures, Scheie Eye Institute, University of Pennsylvania
- 2000 Invited speaker, Society of University Neurosurgeons (Harvard, Brigham and Women's Hospital).
- 2000 Symposium speaker, Third International Symposium on Nucleosides and Nucleotides, Madrid, Spain
- 2000 Symposium speaker, the European College for Neuropsychopharmacology, Munich, Germany
- 2000 Invited Lecture, Case Western Reserve University
- 2000 Invited Lecture, Ohio State University
- 2000 Invited Lecture, Dept. of Brain and Cognitive Sciences, MIT
- 2000 Invited Lecture, Medical College of Pennsylvania-Hahnemann
- 2000 Invited Lecture, Eli Lilly, Indianapolis, IN
- 2001 Invited Lecture, Millenium Pharmaceuticals, Cambridge, MA
- 2001 Plenary Speaker, Chinese Society for Neuroscience, Hong Kong
- 2001 Invited Speaker, NINDS Conference on Re-establishing Circuits in the Damaged Spinal Cord, Bethesda, MD
- 2001 Symposium speaker, American Academy of Anatomists (FASEB), Orlando, FL (Symposium on Brain and Spinal Cord Repair)
- 2001 Symposium speaker, Association for Research in Vision and Ophthalmology, Ft. Lauderdale FL
- 2001 Symposium speaker, International Symposium on Spinal Cord Trauma: Neural Repair and Functional Recovery, Montreal
- 2001 Plenary speaker, Ninth International Neural Regeneration Symposium, Asilomar, California
- 2002 Plenary speaker, "Neuroscience Day", Medical College of Ohio
- 2002 Invited Lecture, Tufts University School of Medicine
- 2002 Invited Lecture, Miami Project to Cure Paralysis, University of Miami, Florida
- 2002 Symposium speaker, Spinal Cord Trauma, Boston Medical Center,
- 2002 Invited speaker, Schepens Eye Institute, Boston
- 2002 Invited speaker, Research to Prevent Blindness, Washington DC
- 2002 Symposium speaker, Third Asia Pacific Symposium on Neural Regeneration, Perth, Australia
- 2003 Visiting Professor, Department of Neurosurgery, University of Pennsylvania
- 2003 Invited speaker, Dept. Physiology, Tufts University School of Medicine

- 2003 Grand Rounds, Longwood Neurology Program, Harvard Med. Sch., Boston
- 2003 Grand Rounds, Department of Neurosurgery, Brigham and Women's Hospital and Children's Hospital, Harvard Medical School

BIBLIOGRAPHY

Journal articles

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2. Benowitz LI, Lee-Teng E (1973) Contrasting effects of three telencephalic ablations on discrimination learning and reversal in chicks. *J Comp Physiol Psychol* 84: 391-397.
3. Benowitz LI, Magnus JG (1973) Memory formation mechanisms following an aversive training experience in chicks. *Behav Biol* 8: 367-380.
4. Benowitz LI, Sperry RW (1973) Amnesic effects of lithium chloride in chicks. *Exp Neurol* 40: 540-546.
5. Benowitz LI (1973) Conditions for the bilateral transfer of monocular learning in chicks. *Brain Res* 65: 203-213.
6. Benowitz LI, Karten HJ (1976) The tractus infundibuli and other afferents to the parahippocampal region of the pigeon. *Brain Res* 102: 174-180.
7. Benowitz LI, Karten HJ (1976) Organization of the tectofugal visual pathway in the pigeon: A retrograde transport study. *J Comp Neur* 167: 503-520.
8. Benowitz LI, Shashoua VE (1977) Localization of a brain protein metabolically associated with behavioral plasticity in the goldfish. *Brain Res* 136: 227-242.
9. Benowitz LI, Shashoua VE (1979) The rapid labeling and secretion of chick brain extracellular proteins. *J Neurochem* 32: 797-809.
10. Benowitz LI, Greene LA (1979) Nerve growth factor in the goldfish brain: Biological assay studies using pheochromocytoma cells. *Brain Res* 162: 164-168.
11. Benowitz LI, Shashoua VE (1979) Immunoreactive sites for nerve-growth factor (NGF) in the goldfish brain. *Brain Res* 172: 561-565.
12. Benowitz LI, Shashoua VE, Yoon MG (1981) Specific changes in rapidly-transported proteins during regeneration of the goldfish optic nerve. *J Neurosci* 1: 300-307.
13. Finklestein S, Benowitz LI, Baldessarini RJ, Arana G, Levine DN, Woo E, Bear DM, Moya KL, Stoll A (1982) Mood, vegetative disturbance, and dexamethasone suppression test after stroke. *Annals of Neurology* 12: 463-468.
14. Benowitz LI, Bear DM, Rosenthal R, Mesulam M-M, Sperry RW, Zaidel E (1983) Hemispheric specialization in nonverbal communication. *Cortex* 19: 5-11.
15. Benowitz LI, Lewis, E (1983) Increased transport of 44-49,000 dalton acidic proteins during regeneration of the goldfish optic nerve: A 2-dimensional gel analysis. *J Neurosci* 3: 2153-2163.
16. Benowitz LI, Yoon MG, Lewis E (1983) Transported proteins in the regenerating optic nerve: Regulation by interactions with the optic tectum. *Science* 222: 185-188

17. Strocchi P, Gilbert JM, Benowitz LI, Dahl D, Lewis ER (1984) The cellular origin and biosynthesis of rat optic nerve proteins: a two-dimensional gel analysis. *J Neurochem* 43: 349-357.
18. Levine DN, Warach JD, Benowitz LI, Calvanio R. (1986) Left spatial neglect: Effects of lesion size and premorbid brain atrophy on severity and recovery following right cerebral infarction. *Neurology* 36: 362-366.
19. Moya KL, Benowitz LI, Levine DN, Finklestein SP (1986) Covariant deficits in story comprehension and visuospatial abilities after right hemisphere stroke. *Cortex* 22: 381-397.
20. Yoon MG, Benowitz LI, Baker F (1986) The optic tectum regulates the transport of specific proteins in regenerating optic fibers of goldfish. *Brain Res* 382: 339-351.
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25. Benowitz LI, Schmidt JT (1987) Activity-dependent-sharpening of the regenerating retinotectal projection in goldfish: relationship to the expression of growth-associated proteins. *Brain Res* 417: 118-126.
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Patents

Larry Benowitz, Carleen Irwin, Paul Jackson, Inventors. Children's Hospital Corp., assignee. Trophic factors for central nervous system regeneration. US Patent 5,898,066. 1999 April 27.

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